UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

Date: April 25, 2018

Subject: **Novaluron.** Occupational and Residential Exposure Assessment for the Proposed New Formulation/Use as an Aerosol for Indoor/Outdoor Environments and Mattresses Applications.

PC Code: 124002
Decision No.: 529840
Petition No.: NA
Risk Assessment Type: Occupational/Residential Exposure Assessment
TXR No.: NA
MRID No.: NA

DP Barcode: D441172
Registration No.: 53883-URL
Regulatory Action: Section 3
Case No.: NA
CAS No.: 116714-46-6
40 CFR: §180.598

From: Joshua Godshall, Biologist
Risk Assessment Branch 1 (RAB1)
Health Effects Division (HED), 7509P

Through: Christine Olinger, Branch Chief
Risk Assessment Branch I (RAB I)
Health Effects Division (7509P)

And

Margarita Collantes, ExpoSAC Reviewer
Monica Hawkins, ExpoSAC Reviewer
Exposure Science Advisory Committee (ExpoSAC)
Health Effects Division (7509P)

To: Eric Bohnenblust, Product Manager Reviewer
Richard Gebken, Acting Product Manager
Invertebrate Branch II (IVB2)
Registration Division (RD; 7505P)

Introduction

The Registration Division (RD) requested that the Health Effects Division (HED) conduct an exposure and risk assessment on novaluron for a new formulated use as an aerosol used in indoor/outdoor commercial and residential environments and mattresses. This assessment examines exposure and risks from novaluron and does not address exposure resulting from additional active ingredients (i.e., deltamethrin or pyriproxyfen) during the use of this product.

Additionally, this document updates the aggregate risk assessment recommendations due to increased exposures assessed in relation to this proposed product.

It is HED policy to use the best available data to assess exposure. Several sources of generic data were used in this assessment as surrogate data in the absence of chemical-specific data, including: Pesticide Handlers Exposure Database Version 1.1 (PHED 1.1); the Outdoor Residential Exposure Task Force (ORETF) database; the Residential SOPs (Indoor Environments). Some of these data are proprietary, and subject to the data protection provisions of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA).

Note: This memorandum was reviewed by the Exposure Science Advisory Committee (ExpoSAC) on April 19, 2018.

Table of Contents

1.0 Executive Summary 4
2.0 Risk Assessment Conclusions and Data Requirements 6
2.1 Summary of Risk Estimates 6
2.2 Label Recommendations 6
2.3 Data Deficiencies and Requirements 6
3.0 Hazard Characterization 6
4.0 Use Profile 9
5.0 Residential Exposure and Risk Estimates 10
5.1 Residential Handler Exposure/Risk Estimates 10
5.2 Residential Post-Application Exposure/Risk Estimates 11
5.3 Residential Risk Estimates for Use in Aggregate Assessment 13
6.0 Non-Occupational Spray Drift Exposure and Risk Estimates 14
7.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates 14
8.0 Occupational Exposure and Risk Estimates 15
8.1 Occupational Handler Exposure/Risk Estimates 15
8.2 Occupational Post-Application Exposure/Risk Estimates 16
8.2.1 Occupational Post-Application Inhalation and Dermal Exposure/Risk Estimates . 17
Appendix A. Summary of Occupational Non-Cancer Algorithms 18

1.0 Executive Summary

Novaluron, a benzolyphenyl urea compound, belongs to the class of insecticides called insect growth regulators. It slowly kills insects by disrupting cuticle formation and depositions causing insect mortality during molting. Novaluron is currently registered for use on several agricultural crops, for use in food- and feed-handling establishments, residential and commercial buildings and structures and their immediate surroundings, on modes of transportation, for indoor (spot/crack and crevice) and outdoor (perimeter) applications for the control of crickets, on pets as a spot-on product for the control of fleas and ticks, as well as mosquito larvicide for use in water bodies or containers that may harbor mosquito larvae.

The proposed product, CSI 16-105 Delta + Tekko Pro Aerosol (EPA Reg. No. 53883-URL), is newly formulated as a ready-to-use (RTU) pressurized liquid (PL) containing 0.2% novaluron in a 16 oz, 17.5 oz, or 20 oz aerosol can. This product also contains 0.06% deltamethrin and 0.02% pyriproxyfen, each of which are assessed in separate documents.

Proposed Use Pattern
The proposed label directs users to apply as an aerosol surface directed broadcast, spot, or crack and crevice treatment for apartments, campgrounds, non-food storage areas, homes, hospitals, hotels, motels, nursing homes, resorts, restaurants and other food handling establishments, schools, supermarkets, transportation equipment (buses, boats, ships, trains, trucks, planes), utilities, warehouses, and other commercial and industrial buildings. The registrant has indicated that aerosol cans will be manufactured in 16 oz, 17.5 oz, and 20 oz cans with an application rate of 0.003 grams novaluron per second of spray.

The proposed new formulation label indicates that the product may be used by occupational/commercial and residential handlers, and does not require specific clothing (e.g., long sleeve shirt/long pants) and/or personal protective equipment (PPE); therefore, the label has been considered in the residential handler assessment for novaluron.

Hazard Characterization
A short-term dermal endpoint was not selected since there were no adverse dermal or systemic effects observed in a 28-day dermal study in rats. Dermal endpoints were previously selected for the intermediate- and long-term scenarios for novaluron; however, a reevaluation of the available data indicates that the toxicity profile for novaluron does not show progression of toxicity with increased duration.

HED identified toxicological points of departure applicable for all durations (i.e., short-, intermediate- and long-term) for the incidental oral and inhalation exposure routes. The no-observed adverse-effect level (NOAEL) for inhalation and incidental oral exposure is 4.38 mg/kg/day for all applicable durations. Novaluron is classified as “not likely to be carcinogenic to humans.”

The level of concern (LOC) for the residential and occupational non-cancer inhalation and incidental oral risk estimates is a margin of exposure (MOE) less than 100 based on the uncertainty factors for inter-species extrapolation (10X), intra-species variation (10X), and the Food Quality Protection Act (FQPA) safety factor for novaluron (reduced to 1X).

Exposure Profile
Occupational and residential dermal and inhalation handler exposures are anticipated for the proposed novaluron use. Residential dermal, inhalation, and incidental oral post-application exposures are expected based on the use pattern of the chemical. Dermal exposures are anticipated; however, a quantitative dermal assessment was not conducted as no toxicological hazard was identified up to the limit dose. Occupational post-application exposures are not anticipated for the proposed use; as commercial applicators do not typically return to the treated areas after an indoor commercial pesticide application. Spray drift is not expected due to the application technique and use site. The durations of inhalation exposure are expected to be short-term (1 to 30 days) for residential handlers and post-application, and short- to intermediate-term (1 to 6 months) for occupational handlers.

Residential Exposures and Risk Estimates
Dermal and inhalation exposures to residential handlers are anticipated for the proposed new aerosol use of novaluron. There are no residential handler inhalation risk estimates of concern (MOEs ≥ 100) for the proposed new uses of novaluron. A quantitative dermal assessment was not conducted as no toxicological hazard was identified up to the limit dose.

Dermal, inhalation, and incidental oral post-application exposures are anticipated for the proposed new aerosol use of novaluron. There are no residential post-application inhalation or incidental oral risk estimates of concern (MOEs ≥ 100) for the proposed new use of novaluron.

Residential Scenarios Recommended for use in Aggregate Assessment
The most protective residential exposure risk estimates have been updated and are included here for inclusion in the aggregate exposure assessment.

- The recommended residential exposure for use in the short-term adult aggregate assessment remains unchanged by this assessment and represents handler inhalation exposure from applications to both indoor and outdoor use sites via manually-pressurized handwand (MOE = 32,000) (L. Venkateshwara, 30-APR-2013, D401261).
- The recommended residential exposure for use in the short-term children 1<2 years old aggregate assessment has been updated in this assessment to reflect combined inhalation and hand-to-mouth exposures to carpet from indoor perimeter/spot/bedbug (coarse & pin stream) applications (MOE = 910) (differs from the MOE of 940 established in *memo*, L. Venkateshwara, 05-FEB-2014, D412298).
- The recommended residential exposure for use in the intermediate- and long term children 1<2 years old aggregate assessment remains unchanged by this assessment and represents post-application hand-to-mouth exposures from the dog spot-on use (MOE = 20,000) (L. Venkateshwara, 21-MAY-2013, D410803).

Occupational Exposures and Risk Estimates
There are no occupational handler inhalation risk estimates of concern (MOEs ≥ 100) for the proposed uses of novaluron with baseline attire (i.e., long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator). Occupational handler dermal exposures are anticipated, however, a quantitative dermal assessment was not conducted as no toxicological hazard was identified up to the limit dose.

Commercial applicators do not typically return to the treated areas after non-agricultural commercial pesticide applications. Based on the Agency's current practices, a quantitative non-cancer occupational post-application inhalation exposure assessment was not performed for novaluron at this time. If new policies or procedures are put into place, the Agency may revisit the need for a quantitative occupational post-application inhalation exposure assessment for novaluron.

Human Studies Review

This risk assessment relies in part on data from studies in which adult human subjects were intentionally exposed to a pesticide or other chemical. These data, which include studies from PHED 1.1; the ORETF database; and the 2012 Residential SOPs (Indoor Environments); are (1) subject to ethics review pursuant to 40 CFR 26, (2) have received that review, and (3) are compliant with applicable ethics requirements. For certain studies, the ethics review may have included review by the Human Studies Review Board. Descriptions of data sources, as well as guidance on their use, can be found at the Agency website[1].

2.0 Risk Assessment Conclusions and Data Requirements

2.1 Summary of Risk Estimates

The residential handler inhalation exposure and risk estimates range from 47,000 to 93,000 and are not of concern (LOC = 100).

The residential post-application inhalation exposure and risk estimate for adults is 360,000 and is not of concern (LOC = 100).

The residential post-application combined inhalation and incidental oral exposure and risk estimates for children 1 to < 2 years old range from 910 to 6,300 and are not of concern (LOC = 100).

The occupational handler inhalation exposure and risk estimate is 11,000 for all use sites and is not of concern (LOC = 100).

2.2 Label Recommendations

None.

2.3 Data Deficiencies and Requirements

None.

3.0 Hazard Characterization

[1] https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data and https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-post-application-exposure

Acute Toxicity

Novaluron has low acute toxicity via the oral, dermal, and inhalation routes (Toxicity Categories III-IV). It is not a dermal irritant, dermal sensitizer, or eye irritant. Table 3.1 presents a summary of the acute toxicity information for novaluron.

Table 3.1. Acute Toxicity of Novaluron.

Guideline No.	Study Type	MRID #(s)	Results	Toxicity Category
870.1100	Acute Oral (rat)	44961001	LD_{50} > 5000 mg/kg	IV
870.1200	Acute Dermal (rat)	45003201	LD_{50} > 2000 mg/kg	III
870.1300	Acute Inhalation (rat)	45003202	LC_{50} > 5.15 mg/L	IV
870.2400	Primary Eye Irritation (rabbit)	45003203	Not an eye irritant	IV
870.2500	Primary Skin Irritation (rabbit)	45003204	Not a dermal irritant	IV
87.2600	Dermal Sensitization (guinea pig)	45084001	Not a dermal sensitizer	N/A

Toxicological PODs Used for Risk Assessment

A dermal endpoint was not selected since there were no adverse dermal or systemic effects observed in a 28-day dermal study in rats. The dermal study specifically looked for blood effects, the target effect for novaluron, and there were no treatment-related effects up to the limit dose. Dermal endpoints were previously selected for the intermediate- and long-term scenarios for novaluron; however, a reevaluation of the available data indicates that the toxicity profile for novaluron does not show progression of toxicity with increased duration. Therefore, there is no concern for any duration of dermal exposure since blood effects were not observed in the 28-day dermal study. Furthermore, there is no concern for susceptibility since no effects were observed in the developmental or reproduction toxicity studies in rats or rabbits.

HED identified toxicological points of departure (PODs) applicable for all durations of incidental oral and inhalation exposure (i.e., short-, intermediate- and long-term). The NOAEL for short- and intermediate-term inhalation and incidental oral exposure is 4.38 mg/kg/day based upon clinical chemical effects (decreased hemoglobin, hematocrit, and red blood cell (RBC) counts) and changes in histopathology (increased hematopoiesis and hemosiderosis in spleen and liver. observed at the lowest-observed adverse-effect level (LOAEL) of 8.64 mg/kg/day in the 90-day rat feeding study. This study is considered protective of the offspring effects observed in the two-generation reproductive study and is thus protective of infants and children in residential settings. Since inhalation and incidental oral exposure routes share a common toxicological endpoint risk estimates may be combined for those routes.

On March 15, 2012, the Hazard and Science Policy Council (HASPOC) concluded, based on a weight of evidence (WOE) approach, that a subchronic inhalation toxicity study was not required (TXR #0052351).[2]

[2] Van Alstine J., 17-APR-2012, TXR #0052351. Novaluron: Summary of Hazard and Science Policy Council (HASPOC) Meeting of March 15, 2012.

HED's LOC for non-cancer risks is defined by uncertainty factors. HED applied a 10X factor to account for inter-species extrapolation and a 10X factor to account for intra-species variation. HED has concluded that the FQPA safety factor for novaluron can be reduced to 1X. A total uncertainty factor (UF) of 100X is applied for all durations of occupational and residential exposure assessment.

Novaluron is classified as "not likely to be carcinogenic to humans."

The toxicity endpoints and the points of departure for various exposure scenarios are presented in Table 3.2.

Table 3.2. Summary of Toxicological Doses and Endpoints for Novaluron for Use in Non-Occupational and Occupational Human-Health Risk Assessments.

Exposure/ Scenario	Point of Departure	Uncertainty/FQPA Safety Factors	LOC for Risk Assessment	Study and Toxicological Effects
Incidental Oral, All Durations	NOAEL= 4.38 mg/kg/day	UF_A = 10X UF_H = 10X FQPA SF = 1X	Residential LOC for MOE = 100	**90-day feeding study in rat** LOAEL = 8.64 mg/kg/day based on clinical chemistry (decreased hemoglobin, hematocrit, and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Dermal, All Durations	A dermal endpoint was not selected since there were no adverse dermal or systemic effects up to the limit dose observed in the 28-day dermal study in rats.			
Inhalation, All Durations	NOAEL= 4.38 mg/kg/day (Inhalation toxicity is assumed to be equivalent via the oral route of exposure.)	UF_A= 10x UF_H=10x FQPA SF= 1x (where applicable)	Residential LOC for MOE = 100 Occupational LOC: MOE = 100	**90-day feeding study in rat** LOAEL = 8.64 mg/kg/day based on clinical chemistry (decreased hemoglobin, hematocrit, and RBC counts) and histopathology (increased hematopoiesis and hemosiderosis in spleen and liver).
Cancer (oral, dermal, inhalation)	Classification: Not likely to be carcinogenic to humans.			

Point of departure = A data point or an estimated point that is derived from observed dose-response data and used to mark the beginning of extrapolation to determine risk associated with lower environmentally relevant human exposures. NOAEL = no-observed adverse-effect level. LOAEL = lowest-observed adverse-effect level. UF = uncertainty factor. UF_A = extrapolation from animal to human (interspecies). UF_H = potential variation in sensitivity among members of the human population (intraspecies). FQPA SF = FQPA Safety Factor. MOE = margin of exposure. LOC = level of concern.

Absorption:
A dermal absorption factor is not needed because there is no hazard identified via the dermal route of exposure. Since inhalation absorption data are not available, toxicity by the inhalation route is considered to be equivalent to the estimated toxicity by the oral route of exposure.

Body Weight
The standard body weight for the general population (80 kg) was used for all adult exposure scenarios covered in this risk assessment since the endpoints selected were not developmental

and/or fetal effects. The standard body weight for children 1 to < 2 years old (11 kg) was used for all children exposure scenarios covered in this risk assessment.

4.0 Use Profile

Novaluron is currently registered for use on several agricultural crops, as well as for use in food- and feed-handling establishments, residential and commercial buildings and structures and their immediate surroundings, and on modes of transportation. Novaluron is also registered for indoor (spot/crack and crevice) and outdoor (perimeter) applications for the control of crickets as well as on pets as a spot-on product for the control of fleas and ticks. The proposed RTU aerosol end-use product is to be applied as a surface directed broadcast, spot, or crack and crevice treatment for apartments, campgrounds, non-food storage areas, homes, hospitals, hotels, motels, nursing homes, resorts, restaurants and other food handling establishments, schools, supermarkets, transportation equipment (buses, boats, ships, trains, trucks, planes), utilities, warehouses, and other commercial and industrial buildings. The registrant has indicated that aerosol cans will be manufactured in 16 oz, 17.5 oz, and 20 oz cans with an application rate of 0.003 grams novaluron per second of spray.

The proposed new formulation product may be used by occupational/commercial and residential handlers, and does not require specific clothing (e.g., long sleeve shirt/long pants) and/or PPE; therefore, the proposed uses have been considered in the residential handler assessment for novaluron. The proposed use pattern is further detailed below in Table 4.1.

Table 4.1. Summary of Directions for the Proposed New Use of Novaluron

Use Site	Application Type	Application Equipment	Max App. Rate[1]	Use Directions and Limitations
CSI 16-105 Delta + Tekko Pro Aerosol (EPA Reg. No. 53883-URL)				
indoor/outdoor residential/commercial environments, transportation equipment, mattresses	commercial food/feed handling establishments	ready-to use aerosol can (0.20% novaluron) 0.0020 lbs ai/16 oz can[2] 0.0022 lbs ai/17.5 oz can 0.0025 lbs ai/20 oz can	1 second spray/spot (1 spot = 2 sq ft)[3]	Hold can 12 to 15 in from surface Do not spray up into air Do not apply to occupied rooms Do not apply to food or food handling surfaces Do not apply in aircraft cabins Do not spray animals directly Repeat treatment as necessary For hospitals/nursing homes: ventilate for two hours after spraying before reoccupying For fleas and ticks: hold can 36 in from surface, and ventilate before reoccupying
	crack and crevice applications		1 linear foot/second 6.6×10^{-6} lbs ai/linear ft	
	spot treatment		1 second spray/2 sq ft 3.3×10^{-6} lbs ai/sq ft (1 spot = 2 sq ft)[3]	
	general surface, fleas and ticks on surfaces		10 seconds/100 sq ft 6.6×10^{-7} lbs ai/sq ft	

1 1-second of spray contains approximately 0.003 grams of novaluron. Application rate used for Deposited Residue = (0.003 g ai/second of spray) × (1 lb ÷ 453.59 g) × (seconds of spray ÷ area sprayed)

2 lbs ai/can = oz can × (1 gal/128 oz) × (8.34 lb/1 gal) × 0.2% novaluron/can [assumes density of water]

3 Per proposed label (EPA Reg. No. 43883-URL) and the 2012 Residential SOPs under Indoor Environments guidance, 1 spot (perimeter/spot/bedbug) = 2 ft^2

5.0 Residential Exposure and Risk Estimates

5.1 Residential Handler Exposure/Risk Estimates

HED uses the term "handlers" to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct tasks related to applications and that exposures can vary depending on the specifics of each task. Residential handlers are addressed somewhat differently by HED as homeowners are assumed to complete all elements of an application without use of any protective equipment.

The proposed novaluron product label lists residential use sites (e.g., indoor environments, hospitals, mattresses, crack and crevices, etc.) that do not require specific clothing (e.g., long sleeve shirt/long pants) and/or personal protective equipment (PPE), and has been considered in the residential handler assessment for novaluron.

Residential Handler Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the residential handler risk assessments. Each assumption and factor is detailed below.

Application Rate:
Maximum application rates as presented in table 4.1 were used to estimate residential handler exposure for the proposed new use.

Unit Exposures and Area Treated or Amount Handled:
Unit exposure values and estimates for area treated or amount handled were taken from HED's 2012 Residential SOPs[3]. As the product will be manufactured in up to 20 oz cans, the amount handled has been updated for the purpose of this assessment from 16 oz cans to 20 oz cans.

Exposure Duration:
Residential handler exposure is expected to be short-term in duration. Intermediate-term exposures are not likely because of the intermittent nature of applications by homeowners.

Residential Handler Non-Cancer Exposure and Risk Estimate Equations
The algorithms used to estimate exposure and dose for residential handlers can be found in the 2012 Residential SOPs[4].

Combining Exposures/Risk Estimates:
Residential handler dermal and inhalation exposure is anticipated from the proposed novaluron use, however there is no dermal hazard for novaluron. Therefore, only inhalation exposures have been quantitatively assessed and there are no additional routes to combine.

[3] Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide
[4] Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Summary of Residential Handler Non-Cancer Exposure and Risk Estimates

The residential handler inhalation exposure and risk estimate MOEs range from 47,000 to 93,000 and are not of concern (LOC = 100). The inhalation risks for residential handlers are presented in Table 5.1.1 below.

Table 5.1.1. Residential Handler Non-Cancer Exposure and Risk Estimates for Novaluron.

Exposure Scenario	Equipment	Inhalation Unit Exposure[1] (mg/lb ai)	Maximum Application Rate[2]	Area Treated or Amount Handled Daily[3]	Inhalation	
					Dose (mg/kg/day)[4]	MOE[5] (LOC = 100)
Mixer/Loader/Applicator						
Indoor environment, broadcast surface spray	ready-to-use aerosol can (20 oz)	3	0.0025 lbs ai/20 oz can	1-20 oz can	0.000094	47,000
Indoor/outdoor environments, perimeter/spot/bedbug (course application)				1/2-20 oz can	0.000047	93,000
Indoor/outdoor environments, perimeter/spot/bedbug (pinstream application); crack and crevice					0.000047	93,000

1 Based on proposed label (EPA Reg. No. 43883-URL) as detailed in Table 4.1.
2 Registrant indicated largest can produced using this label will be 20 oz.
3 Based on HED's 2012 Residential SOPs (http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide), as well as information provided by the registrant.
4 Inhalation Dose = Inhalation Unit Exposure (mg/lb ai) × Application Rate (lb ai/acre or gal) × Area Treated or Amount Handled (A/day or gallons/day) ÷ BW (80 kg).
5 Inhalation MOE = Inhalation NOAEL (4.38 mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

5.2 Residential Post-Application Exposure/Risk Estimates

There is the potential for post-application exposure for individuals exposed as a result of being in an environment that has been previously treated with novaluron. The quantitative exposure/risk assessment for residential post-application exposures is based on the following scenarios:

- Children 1 to <2 years old incidental oral (hand to mouth and object to mouth) post-application exposures from contact with treated carpet and hard flooring following indoor broadcast, crack and crevice, and perimeter/spot/bedbug applications.
- Adult inhalation post-application exposures following indoor aerosol surface directed broadcast, spot, and crack and crevice applications.
- Children 1 to <2 years old inhalation post-application exposures following indoor aerosol surface directed broadcast, spot, and crack and crevice applications.

The lifestages selected for each post-application scenario are based on an analysis provided as an Appendix in the 2012 Residential SOPs[5]. While not the only lifestage potentially exposed for these post-application scenarios, the lifestage that is included in the quantitative assessment is health protective for the exposures and risk estimates for any other potentially exposed lifestage.

[5] Available: http://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide

Residential Post-Application Exposure Data and Assumptions

A series of assumptions and exposure factors served as the basis for completing the residential post-application risk assessment. Each assumption and factor is detailed in the 2012 Residential SOPs[5].

Application Rate:

Maximum application rates as presented in table 4.1 were used to estimate residential post-application exposure for the proposed new uses. The proposed label identified unique application rates for each application type (broadcast, perimeter/spot/bedbug, and crack and crevice) which were independently incorporated into this assessment to establish deposited residue values.

Deposited Residue: Based on the 2012 SOPs, the deposited residue from indoor broadcast applications was determined using a tiered approach. Since chemical-specific deposited residue data were not available, a deposited residue value was calculated for aerosol applications to indoor areas using label provided information (i.e., 1 second of spray contains approximately 0.003 grams of novaluron). This resulted in deposited residue values for broadcast (0.32 $\mu g/cm^2$), perimeter/spot/bedbug – coarse/pin stream (0.81 $\mu g/cm^2$), and crack/crevice (0.32 $\mu g/cm^2$) applications using their respective application rates identified in Table 4.1.

Chemical Properties: Post-application inhalation exposures were quantitatively assessed using chemical and product specific information including the molecular weight (492.71 g/mol) and vapor pressure (1.2×10^{-7} mmHg) (S. Levy, 03-NOV-2005, D315780).

Exposure Duration: Residential post-application exposure is expected to be short -term in duration. Longer-term exposures are not likely due to the seasonal nature of applications by homeowners as indicated by the representative labels.

Residential Post-Application Non-Cancer Exposure and Risk Equations

The algorithms used to estimate residential post-application exposure and dose can be found in the 2012 Residential SOPs.

Combining Exposures/Risk Estimates:

Residential post-application dermal, incidental oral, and inhalation exposure is anticipated from the proposed novaluron uses, however there is no dermal hazard for novaluron. Since inhalation and incidental oral exposure routes share a common toxicological endpoint for children (1 to <2 years old), risk estimates have been combined for those routes. The incidental oral scenarios (i.e., hand-to-mouth and object-to-mouth) should be considered inter-related and it is likely that they occur interspersed amongst each other across time.

Summary of Residential Post-Application Non-Cancer Exposure and Risk Estimates

The residential post-application inhalation exposure and risk estimate MOE for adults is 360,000. The residential post-application combined inhalation and incidental oral exposure and risk estimate MOEs for children 1 to < 2 years old range from 910 to 6,300 and are not of concern (LOC = 100). All risks for residential post-application are presented in Table 5.2.1 below.

Table 5.2.1. Residential Post-Application Non-Cancer Exposure and Risk Estimates for Novaluron.							
Lifestage	**Post-application Exposure Scenario**		**Application Rate[1] Deposited Residue[2]**	**Dose (mg/kg/day)[2]**	**MOEs[3]**	**Combined Routes**	**Combined MOEs[4]**
	Use Site	**Route of Exposure**					
Adult	Indoor Surface Directed	Inhalation	0.0025 lbs ai/20 oz can	0.000012	360,000	N/A	N/A
Child		Inhalation		0.000053	83,000	N/A	N/A
Child 1 to <2 years old	Indoor Broadcast - Carpet	HtM	6.61×10^{-7} lbs ai/ft^2	0.0019	2,300	w/ Inhalation	2,200
		OtM		0.00025	17,000	N/A	N/A
	Indoor Broadcast – Hard Surface	HtM	Deposited Residue 0.32 ug/cm^2	0.00064	6,900	w/ Inhalation	6,300
		OtM		0.00017	26,000	N/A	N/A
	Indoor Perimeter/Spot/Bedbug (Coarse & Pin Stream) - Carpet	HtM	6.61×10^{-6} lbs ai/ft^2	0.0048	920	w/ Inhalation	910
		OtM		0.00063	6,900	N/A	N/A
	Indoor Perimeter/Spot/Bedbug (Coarse & Pin Stream) – Hard Surface	HtM	Deposited Residue 0.81 ug/cm^2	0.0016	2,800	w/ Inhalation	2,700
		OtM		0.00042	10,000	N/A	N/A
	Indoor Crack and Crevice - Carpet	HtM	6.61×10^{-6} lbs ai/linear ft	0.0019	2,300	w/ Inhalation	2,200
		OtM		0.00025	17,000	N/A	N/A
	Indoor Crack and Crevice – Hard Surface	HtM	Deposited Residue 0.32 ug/cm^2	0.00064	6,900	w/ Inhalation	6,300
		OtM		0.00017	26,000	N/A	N/A

1 Based on proposed labels (Reg. No. 53883-URL). Application rate used for Deposited Residue = (0.003 g ai/second of spray) × (1 lb ÷ 453.59 g) × (seconds of spray ÷ area sprayed)
2 Dose (mg/kg/day) algorithms provided in 2012 Residential SOPs (https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/standard-operating-procedures-residential-pesticide).
3 MOE = POD (mg/kg/day) ÷ Dose (mg/kg/day).
4 Combined MOE = 1 ÷ [(1/inhalation MOE) + (1/incidental oral MOE)], where applicable.

5.3 Residential Risk Estimates for Use in Aggregate Assessment

In accordance with the FQPA, HED must consider and aggregate novaluron pesticide exposures and risk from three major sources: food, drinking water, and residential exposures. In an aggregate assessment, exposures from relevant sources are added together and compared to quantitative estimates of hazard (e.g., a NOAEL or PAD), or risks themselves can be aggregated. **Note:** The children 1 to < 2 years old short-term aggregate assessment MOE has been updated as a result of the risks identified in this assessment (differs from risk established in memo, L. Venkateshwara, 05-FEB-2014, D412298). Table 5.3.1 reflects the residential risk estimates that are recommended for use in the aggregate assessment for novaluron.

- The recommended residential exposure for use in the short-term adult aggregate assessment reflects handler inhalation exposure from applications to both indoor and outdoor use sites via manually-pressurized handwand (L. Venkateshwara, 30-APR-2013, D401261).
- The recommended residential exposure for use in the short-term children 1<2 years old aggregate assessment reflect combined inhalation and hand-to-mouth exposures to carpet from indoor perimeter/spot/bedbug (coarse & pin stream) applications.
- The recommended residential exposure for use in the intermediate- and long-term children 1<2 years old aggregate assessment reflects post-application hand-to-mouth exposures from the dog spot-on use (L. Venkateshwara, 21-MAY-2013, D410803).

Table 5.3.1. Recommendations for the Residential Exposures for the Novaluron Aggregate Assessment.									
Lifestage	Exposure Scenario	Dose (mg/kg/day)[1]				MOE[2]			
		Dermal	Inhalation	Oral	Total	Dermal	Inhalation	Oral	Total
Short -Term									
Adult	Handler application to in/outdoor sites	NA	0.00014	N/A	0.00014	NA	32,000	N/A	32,000
Child 1 to < 2 years old	Post-application: Indoor Carpet perimeter/spot/bedbug (coarse & pin stream)		0.000053	0.00478	0.00483		83,000	910	910
Intermediate- and Long-Term									
Child 1 to < 2 years old	Post-application: HtM pet spot-on	N/A	N/A	0.00022	0.00022	N/A	N/A	20,000	20,000

1 Dose = the highest dose for each applicable lifestage of all residential scenarios assessed. Total = dermal + inhalation + incidental oral (where applicable).

2 MOE = the MOEs associated with the highest residential doses. Total = 1 ÷ (1/Dermal MOE) + (1/Inhalation MOE) + (1/Incidental Oral MOE), where applicable

6.0 Non-Occupational Spray Drift Exposure and Risk Estimates

Spray drift is a potential source of exposure to those nearby pesticide applications. This is particularly the case with aerial application, but, to a lesser extent, spray drift can also be a potential source of exposure from the ground application methods (e.g., groundboom and airblast) employed for novaluron. The agency has been working with the Spray Drift Task Force (a task force composed of various registrants which was developed as a result of a Data Call-In issued by EPA), EPA Regional Offices and State Lead Agencies for pesticide regulation and other parties to develop the best spray drift management practices (see the agency's Spray Drift website for more information).[6] The agency has also developed a policy on how to appropriately consider spray drift as a potential source of exposure in risk assessments for pesticides. The potential for spray drift will be quantitatively evaluated for each pesticide during the *Registration Review* process which ensures that all uses for that pesticide will be considered concurrently. The approach is outlined in the revised (2012) *Standard Operating Procedures for Residential Risk Assessment (SOPs) - Residential Exposure Assessment Standard Operating Procedures Addenda 1: Consideration of Spray Drift.* This document outlines the quantification of indirect non-occupational exposure to drift.

Although a quantitative spray drift assessment will be conducted at the time of Registration Review for all registered uses of novaluron, the proposed ready-to-use formulation is unlikely to result in non-occupational bystander exposures from spray drift due to the application technique and indoor use site.

7.0 Non-Occupational Bystander Post-Application Inhalation Exposure and Risk Estimates

Per the Residential SOPs, a quantitative residential post-application inhalation exposure assessment was performed in the residential post-application section of the ORE chapter (Section 5.2).

[6] Available: http://www.epa.gov/reducing-pesticide-drift

8.0 Occupational Exposure and Risk Estimates

8.1 Occupational Handler Exposure/Risk Estimates

HED uses the term handlers to describe those individuals who are involved in the pesticide application process. HED believes that there are distinct job functions or tasks related to applications and exposures can vary depending on the specifics of each task. Job requirements (amount of chemical used in each application), the kinds of equipment used, the target being treated, and the level of protection used by a handler can cause exposure levels to differ in a manner specific to each application event.

Based on the anticipated use patterns and current labeling, types of equipment and techniques that can potentially be used, occupational handler exposure is expected from the proposed uses. The quantitative exposure/risk assessment developed for occupational handlers is based on the scenarios listed in Table 8.1.1.

Occupational Handler Exposure Data and Assumptions
A series of assumptions and exposure factors served as the basis for completing the occupational handler risk assessments. Each assumption and factor is detailed below on an individual basis.

Application Rate: Maximum application rates as presented in table 4.1 were used to estimate occupational handler exposure for the proposed new uses.

Unit Exposures: It is the policy of HED to use the best available data to assess handler exposure. Sources of generic handler data, used as surrogate data in the absence of chemical-specific data, include PHED 1.1. Some of these data are proprietary and subject to the data protection provisions of FIFRA. The standard values recommended for use in predicting handler exposure that are used in this assessment, known as "unit exposures", are outlined in the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table[7]", which, along with additional information on HED policy on use of surrogate data, including descriptions of the various sources, can be found at the Agency website[8].

Area Treated or Amount Handled:
10 cans of product per day.

Exposure Duration: HED classifies exposures from 1 to 30 days as short-term and exposures 30 days to six months as intermediate-term. Exposure duration is determined by many things, including the exposed population, the use site, the pest pressure triggering the use of the pesticide, and the cultural practices surrounding that use site.

For the proposed novaluron uses, short- and intermediate-term exposures are expected based on the proposed use patterns. Since the PODs selected for short- and intermediate-term inhalation

[7] Available: https://www.epa.gov/sites/production/files/2016-11/documents/handler-exposure-table-2016.pdf
[8] Available: https://www.epa.gov/pesticide-science-and-assessing-pesticide-risks/occupational-pesticide-handler-exposure-data

exposures are the same for both durations, the assessment is protective of both short- and intermediate-term occupational exposures.

Mitigation/Personal Protective Equipment: Estimates of dermal and inhalation exposure were calculated for baseline levels of PPE, defined as a single layer of clothing consisting of a long sleeved shirt, long pants, shoes plus socks, no protective gloves, and no respirator. The proposed novaluron product label does not direct mixers, loaders, applicators and other handlers to wear any specific clothing or PPE.

Combining Exposures/Risk Estimates:
Occupational handler dermal and inhalation exposure is anticipated from the proposed novaluron use, however no dermal hazard has been observed for novaluron. Therefore, only inhalation exposures have been quantitatively assessed and there are no additional routes to combine.

Occupational Handler Non-Cancer Exposure and Risk Estimate Equations
The algorithms used to estimate non-cancer exposure and dose for occupational handlers can be found in Appendix A.

Summary of Occupational Handler Non-Cancer Exposure and Risk Estimates
The occupational handler inhalation exposure and risk estimate MOE is 11,000 for all use sites and is not of concern (LOC = 100). The inhalation risks for occupational handlers are presented in Table 8.1.1.

Table 8.1.1. Occupational Handler Non-Cancer Exposure and Risk Estimates for Novaluron.

Exposure Scenario	Crop or Target	Inhalation Unit Exposure (µg/lb ai)[1]	Maximum Application Rate[2]	Area Treated Daily[3]	Inhalation	
		No Respirator			Dose (mg/kg/day)[4]	MOE[5] (LOC=100)
Applicator						
RTU aerosol can surface directed broadcast, crack and crevice, spot applications	Commercial/industrial/ residential indoor and outdoor perimeter environments	1,300	0.0025 lbs ai/20 oz can	10 cans	0.00041	11,000

1 Based on the "Occupational Pesticide Handler Unit Exposure Surrogate Reference Table" (November 2016); Level of mitigation: Baseline, PPE (long sleeve shirt, long pants, shoes plus socks, no-gloves, no-respirator).
2 Based on proposed labels summarized in Table 4.1 (Reg. No. 53883-URL).
3 (J. Tyler, 07-DEC-2016, D436501) and Exposure Science Advisory Council Policy #9.1
4 Inhalation Dose = Inhalation Unit Exposure (µg/lb ai) × Conversion Factor (0.001 mg/µg) × Application Rate (lb ai/acre or gal) × Area Treated Daily (A or gal/day) ÷ BW (80 kg).
5 Inhalation MOE = Inhalation NOAEL (mg/kg/day) ÷ Inhalation Dose (mg/kg/day).

8.2 Occupational Post-Application Exposure/Risk Estimates

HED uses the term post-application to describe exposures that occur when individuals are present in an environment that has been previously treated with a pesticide (also referred to as re-entry exposure). Such exposures may occur when workers enter previously treated areas to perform job functions, including activities related to crop production, such as scouting for pests or harvesting. Post-application exposure levels vary over time and depend on such things as the

type of activity, the nature of the crop or target that was treated, the type of pesticide application, and the chemical's degradation properties. In addition, the timing of pesticide applications, relative to harvest activities, can greatly reduce the potential for post-application exposure.

8.2.1 Occupational Post-Application Inhalation and Dermal Exposure/Risk Estimates

Commercial applicators do not typically return to the treated areas after non-agricultural commercial pesticide applications (sites such as warehouses, food handling establishments, treated residential homes, and hotels, etc.) and thus an occupational post-application inhalation and dermal exposure assessment was not performed for commercial applicators. Additionally, no hazard was identified for dermal exposure up to the limit dose; therefore, a quantitative dermal post-application exposure assessment was not conducted.

Appendix A. Summary of Occupational Non-Cancer Algorithms

Occupational Non-Cancer Handler Algorithms

Potential daily exposures for occupational handlers are calculated using the following formulas:

$$E = UE * AR * A * 0.001\ mg/ug$$

where:

E	=	exposure (mg ai/day),
UE	=	unit exposure (µg ai/lb ai),
AR	=	maximum application rate according to proposed label (lb ai A or lb ai/gal), and
A	=	area treated or amount handled (e.g., A/day, gal/day).

The daily doses are calculated using the following formula:

$$ADD = \frac{E * AF}{BW}$$

where:

ADD	=	average daily dose absorbed in a given scenario (mg ai/kg/day),
E	=	exposure (mg ai/day),
AF	=	absorption factor (dermal and/or inhalation), and
BW	=	body weight (kg).

Margin of Exposure: Non-cancer risk estimates for each application handler scenario are calculated using a Margin of Exposure (MOE), which is a ratio of the toxicological endpoint to the daily dose of concern. The daily dermal and inhalation dose received by occupational handlers are compared to the appropriate POD (i.e., NOAEL) to assess the risk to occupational handlers for each exposure route. All MOE values are calculated using the following formula:

$$MOE = \frac{POD}{ADD}$$

where:

MOE	=	margin of exposure: value used by HED to represent risk estimates (unitless),
POD	=	point of departure (mg/kg/day), and
ADD	=	average daily dose absorbed in a given scenario (mg ai/kg/day).